glucocorticoid, or with vehicle as a control, NTC cells had 2039 Dex-regulated genes, while Dex was still able to regulate 1087 genes in GRKD cells. Of these 1087 genes, 895 genes were uniquely regulated by Dex in GRKD cells suggesting that glucocorticoids might be signaling through another receptor in corneal epithelial cells. The top canonical pathways predicted to be altered by Dex in GRKD cells included PI3K/ATK Signaling, ERK5 Signaling, Prostrate Cancer Signaling, Aldosterone Signaling in Epithelial Cells, and PPAR signaling. These findings suggest that Dex could regulate large cohorts of genes through other nuclear receptors in corneal epithelial cells. Given the wide use of ophthalmic Dex in forms including eyedrops, ointments, gels, and implants, it is of clinical significance to understand the molecular actions of synthetic glucocorticoids since they appear to be ligands for multiple nuclear receptors in ocular cells and tissues.

Steroid Hormones and Receptors

STEROID HORMONES, NUCLEAR RECEPTORS, AND COLLABORATORS

Glucocorticoid Receptor Condensates Link DNA-Dependent Receptor Dimerization and Transcriptional Transactivation

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The glucocorticoid receptor (GR) is a ligand-regulated transcription factor (TF) that controls the tissue- and gene-specific transactivation and transrepression of thousands of target genes. Distinct GR DNA binding sequences with activating or repressive activities have been identified, but how they modulate transcription in opposite ways is not known. We show that GR forms phase-separated condensates that specifically concentrate known co-regulators via their intrinsically disordered regions (IDRs) in vitro. A combination of dynamic, multivalent (between IDRs) and specific, stable interactions (between LxxLL motifs and the GR ligand binding domain) control the degree of recruitment. Importantly, GR DNA-binding directs the selective partitioning of co-regulators within GR condensates such that activating DNAs cause enhanced recruitment of co-activators. Our work shows that condensation controls GR function by modulating co-regulator recruitment and provides a mechanism for the up- and down-regulation of GR target genes controlled by distinct DNA recognition elements.

Steroid Hormones and Receptors

STEROID HORMONES, NUCLEAR RECEPTORS, AND COLLABORATORS

Improving the Diagnosis, Treatment, and Prevention of Endocrine Diseases Through Accurate and Reliable Laboratory Measurements With CDC Clinical Standardization Programs

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Laboratory measurements are critical for correct diagnosis and treatment of patients with chronic diseases such as hypogonadism, PCOS, and thyroid diseases. Inaccurate measurements of disease biomarkers can lead to misclassification of patients/incorrect treatment and prevent the effective use of research findings in patient care. The CDC Clinical Standardization Programs (CDC CSP) improve the accuracy and reliability of clinical biomarker measurements by assessing and improving the analytical performance of assays. The CDC CSP assist with assay calibration, the certification of analytical performance, and the monitoring of routine patient and research testing. The CDC CSP work with clinical/research laboratories and assay manufacturers to improve laboratory measurements. Its current programs include the following analytes: total testosterone (TT), estradiol (E2), vitamin D (VD), free thyroxine (FT4), total cholesterol (TC), total glycerides (TG), HDL-cholesterol (HDL-C), and LDL-cholesterol (LDL-C). The work is being conducted through certification/monitoring programs and technical assistance. Most assays participating in the certification programs have seen performance improvements and maintain performance over time by continuous participation. Most major commercial laboratories and assays manufactures are enrolled in the certification programs. Currently certified and non-certified assays are available. Assays certified by CDC CSP are listed on the website at https://www.cdc.gov/labstandards/hs.html. The CDC Lipid Standardization Programs and CDC Accuracy-based Monitoring Programs allow for weekly monitoring of analytical performance of routine tests for analytes including TT, VD, TC, TG, HDL-C, apolipoprotein A1 and B. These monitoring programs assist researchers with assessing measurement accuracy of research studies over time and across laboratories. The CDC CSP also support accuracy-based external quality assurance surveys such as those offered by the College of American Pathologists (CAP). The CDC CSP assist researchers and stakeholders with developing and establishing reference intervals and conducting studies to better assess and diagnose patients. Based on the needs and requests from clinical community, programs for new biomarkers such as Lp(a), PTH and glucose are being developed. The CDC CSP work with stakeholders, such as the Endocrine Society and the Partnership for the Accurate Testing of Hormones, to educate the clinical and laboratory communities about the importance of using standardized assays in patient care, research, and public health.

Steroid Hormones and Receptors

STEROID HORMONES, NUCLEAR RECEPTORS, AND COLLABORATORS

Inhibition of Estrogen Signaling Reverses Established Inguinal Hernias

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